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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,321	02/17/2004	Roland Buelow	A-64360-2/TAL/NHT	1116

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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 08/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/780,321	BUELOW ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,11-15,18-21 and 29-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11-15,18-21 and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Prosecution on this case is HEREBY REOPENED.

2. Applicant's amendment filed 8/7/06 is acknowledged and has been entered.

Claims 1-8, 11-15, 18-21 and 29-31 are pending and are presently being examined.

Applicant is reminded that the following issues remain.

3. Applicant is required under 37 C.F.R. 1.821(d) to amend the specification to list the appropriate SEQ ID NO for sequences disclosed in the specification (for example, in the brief description of the drawings for the sequence shown in the figures).

Applicant is reminded that Applicant's amendment filed 7/5/06 was not entered.

4. Applicant is reminded that with regard to Applicant's amendment to the specification filed 8/16/04, the direction to amend the specification at paragraph numbers appears to be off by one paragraph number, *i.e.,* for example, the replacement paragraph [0008] that Applicant directs be replaced, is actually paragraph [0009] in the specification, and so forth for the other replacement paragraphs.

Applicant is reminded that Applicant's amendment filed 7/5/06 was not entered.

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-8, 11-15, 18-21 and 29-31 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 9 and 10 of copending Application No. 10/376,647 in view of U.S. Patent No. 5,702,946 A, WO 93/03764 and U.S. Patent No. 6,828,415 B2.

This is a provisional obviousness-type double patenting rejection.

Claims 9 and 10 of copending Application No. 10/376,647 are drawn to a pharmaceutical composition for reducing gastrointestinal toxicity induced by cytoablative therapy comprising the peptide recited in instant claim 1 and further comprising an agent that is one of an anti-diarrheal agent, an anti-inflammatory agent or an analgesic agent, and in the case of claim 10, to an anti-diarrheal agent.

Claims 9 and 10 of copending Application No. 10/376,647 do not recite wherein a pharmaceutically acceptable medium is an excipient that is mannitol, nor wherein the oligopeptide has the structural formula recited in instant claim 7, *i.e.,* has D-amino acid residues except at position 9.

U.S. Patent No. 5,702,946 A discloses pharmaceutical compositions comprising polypeptides that are antibodies to IL-8 that are used to treat inflammatory disorders such as organ failure, septic shock ARDS, IBD and bacterial pneumonia, said pharmaceutical compositions comprising mannitol (especially abstract and column 14 at lines 1-21).

WO 93/03764 teaches that peptides are more stable when the D-amino acid form is used and that the peptide sequences can be modified by carboxy terminal amidation or other modifications at the carboxy or amino termini (especially page 17 at lines 27-37 page 4 at lines 28-33, page 15 at lines 10-24).

U.S. Patent No. 6,828,415 B2 discloses a decapeptide with a terminal acid amide group that is used in the form of its acetate salt for pharmaceutical administration (especially column 1 at lines 10-15).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have formulated the peptide recited in claims 9 and 10 of '647 in a pharmaceutical composition comprising the excipient mannitol as disclosed by U.S. Patent No. 5,702,946 A, to have made the peptide with any or all of the amino acid residues as the D-amino acid form, and to have formulated the peptide as a carboxy-terminal amide as taught by WO 93/03764 or to have formulated it as the acetate salt of an amide as disclosed by U.S. Patent No. 6,828,415 B2. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made a carboxy-terminal amide version of the oligopeptide as taught by WO 93/03764 or acetate salt of an amide as disclosed by U.S. Patent No. 6,828,415 B2 at the carboxy-terminal position.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to inhibit T cell proliferation and T cell mediated lysis, *i.e.,* forms of inflammation, because U.S. Patent No. 5,702,946 A discloses pharmaceutical compositions comprising other polypeptides that are anti-inflammatory agents in a pharmaceutical composition comprising the excipient mannitol, and one of ordinary skill in the art at the time the invention was made would have been motivated to have used the L amino acid residue form of the peptide or to have substituted D-amino acid residues at any or all positions in the oligopeptide. One of ordinary skill in the art at the time the invention was made would have been motivated to have made the acetate salt of an amide or amide versions of the oligopeptide because WO 93/03764 teaches formulating peptides as carboxy-terminal amides and U.S. Patent No. 6,828,415 B2 discloses making an acetate salt of an amide for use in pharmaceutical compositions.

In addition, the oligopeptides of instant claims 1-7 and 11-28 are encompassed by the composition comprising the said oligopeptide of copending Application No. 10/376,647, and the composition comprising the oligopeptides of instant claims 8 and 29-31 encompass the composition of claims 9 and 10 of copending Application No. 10/376,647.

7. Claims 1-8, 11-15, 18-21 and 29-31 are directed to an invention not patentably distinct from claims 9 and 10 of commonly assigned copending Application No. 10/376,647, as enunciated supra at item #6 of this Action.

8. The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned 10/376,647, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

The following are new grounds of rejection.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-8, 11-15, 18-21 and 29-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of the claimed oligopeptide and pharmaceutical composition thereof recited in the instant claims.

The instant claims encompass an oligopeptide and pharmaceutical composition thereof *comprising* SEQ ID NO: 13, including the D amino acid forms and the salt and/or amidated forms recited in the dependent claims. There is insufficient disclosure in the specification on such a composition, *i.e.,* one that *comprises* SEQ ID NO: 13 and has undisclosed N- and/or -C terminal flanking sequences.

As to the issue of "*comprises*", the specification does not disclose an oligopeptide *comprising* SEQ ID NO: 13, but rather one that consists of SEQ ID NO: 13.

The instant specification discloses that the immunosuppressive peptides of the invention, including SEQ ID NO: 13, exhibit a well defined common conformational space ([0081]). The instant specification further discloses that 2702.75-84 peptide (RENLRIALRY) was used as a teaching construct in the development of the peptides of the invention, including SEQ ID NO: 13, in that the said peptides satisfy the parameters of Tables 1 (and 2, for SEQ ID NO: 13), and was shown to have activity regulating T-cells ([0074]-[0079]).

Evidentiary reference Grassy *et al* teach 10-mer derivatives of the 2702.75-84 peptide (RENLRIALRY), five of which were tested and four of which displayed activity in prolonging graft survival in mice, that the conformation of the peptide is important for biological activity, and further that the active peptides may require the ability to form a loop (especially last column on page 751, Applicant's IDS reference "C12" in the Form 1449 filed 8/16/04).

Evidentiary reference WO 95/13288 (Applicant's IDS reference "B6" in the form 1449 filed 8/16/04) teaches a peptide comprising the HLA-B2702.60-84 peptide that blocks CTL lysis, and further comprising a peptide that does not possess the inhibitory activity (especially pages 9-11), and that the B2702.60-84 peptide alone when conjugated to BSA lost activity (especially page 12).

The relationship between the sequence of a peptide and its tertiary structure (*i.e.,* its activity) are not well understood and are not predictable (see evidentiary reference Ngo *et al,* Applicant's IDS reference "C18" in the Form 1449 filed 8/16/04).

The instant disclosure does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera, including any undisclosed N- and/or –C terminal flanking sequence. Since the disclosure fails to provide sufficient relevant identifying characteristics, and because the genus is highly variant, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

11. Claims 1-8, 11-15, 18-21 and 29-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not disclose how to make and use the instant invention, an oligopeptide *comprising* SEQ ID NO: 13 and pharmaceutical composition thereof, including those comprising the amidated and/or salt forms of SEQ ID NO: 13 recited in the dependent claims.

The specification has not enabled the breadth of the claimed invention because the claims encompass an oligopeptide *comprising* SEQ ID NO: 13 and amidated and/or salt forms thereof and pharmaceutical composition thereof that contains undisclosed N- and/or –C terminal flanking sequences. The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the claimed oligopeptide and composition thereof can be made and/or used.

As to the issue of "*comprises*", the specification does not disclose an oligopeptide *comprising* SEQ ID NO: 13, but rather one that consists of SEQ ID NO: 13.

The instant specification discloses that the immunosuppressive peptides of the invention, including SEQ ID NO: 13, exhibit a well defined common conformational space ([0081]). The instant specification further discloses that 2702.75-84 peptide (RENLRIALRY) was used as a teaching construct in the development of the peptides of the invention, including SEQ ID NO: 13, in that the said peptides satisfy the parameters of Tables 1 (and 2, for SEQ ID NO: 13), and was shown to have activity regulating T-cells ([0074]-[0079]).

Evidentiary reference Grassy *et al* (Applicant's IDS reference "B6" in the form 1449 filed 8/16/04) teach 10-mer derivatives of the 2702.75-84 peptide (RENLRIALRY), five of which were tested and four of which displayed activity in prolonging graft survival in mice, that the conformation of the peptide is important for biological activity, and further that the active peptides may require the ability to form a loop (especially last column on page 751, Applicant's IDS reference "C12" in the Form 1449 filed 8/16/04).

Evidentiary reference WO 95/13288 teaches a peptide comprising the HLA-B2702.60-84 peptide that blocks CTL lysis, and further comprising a peptide that does not possess the inhibitory activity (especially pages 9-11), and that the B2702.60-84 peptide alone when conjugated to BSA lost activity (especially page 12).

The relationship between the sequence of a peptide and its tertiary structure (*i.e.,* its activity) are not well understood and are not predictable (see evidentiary reference Ngo *et al,* Applicant's IDS reference "C18" in the Form 1449 filed 8/16/04).

There is insufficient guidance in the specification as to how to make and/or use instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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